UNITED STATES DEPARTMENT OF COMMERCE
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09/205,096 12/03/98 DRACHMAN

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| | | | 737 |

HM12/1206

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| EXAMINER |
|---|
| SURREY, E |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

DATE MAILED: 12/12/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

File Copy

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/205,096 | DRACHMAN, DANIEL B. | |
| | Examiner | Art Unit | |
| | Eleanor Sorbello | 1633 | |

*-- The MAILING DATE of this communication appears on th cover sh et with the correspond nc address --*

**Peri d for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *4,5,9-12,14,19,22,28,31,35 and 41-67* is/are pending in the application.

4a) Of the above claim(s) *4,5,9-12,14,19,22,28,31,35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

**Attachment(s)**

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

***Response to amendm nt***

1. Applicant's amendment and response to the official Office Action mailed May 25, 2000 as Paper No. 10, has been received and filed on October 02, 2000 as Paper No. 12. Claims 1-3, 6-8, 13, 15-18, 20, 21, 23-27, 29, 30, 32-34 and 36-40 have been canceled, and claims 41-67 have been added. Claims 4, 5, 9-12, 14, 19, 22, 28, 31, 35 and 41-67 are pending. Claims 4, 5, 9-12, 14, 19, 22, 28, 31and 35 stand withdrawn. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the new claims and/or applicant's argument.

2. Applicant's arguments are addressed below on a per section basis. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 41-67 stand rejected under 35 USC § 112, first paragraph for the same reasons of record. Applicant's new claims do not change the context of gene therapy necessarily as argued in FOAM, and arguments have been fully considered but they are not found persuasive. The preamble of the new claims recite "a method of ablating autoantigen specific T cells" rather than "a method of activating autoantigen specific T cells", yet the claims remain directed to gene therapy (as they both include in their methods, the reintroduction of the APCs comprising a nucleotide into a patient), because the nature and scope of the claims are not changed necessarily.

Applicant's have argued that ex vivo therapy is different and does not fall in the realm of gene therapy. However, introduction of a gene into a patient, by first introducing the gene into cells ex vivo and subsequently introducing the transformed cells into a patient is considered gene therapy. Contrary to applicant's argument, Orkin et al. have referred to the transfer of DNA into recipient cells, from outside the body as ex vivo therapy, and referred to in the section titled, "issues of gene therapy". (See Orkin, page 7, "Basic science issues in gene therapy", line 5).

Crystal et al. in his review article pointed out different strategies by which gene transfer is carried out and stated that the choice of an *ex-vivo* or *in vivo* strategy and of the vector is dictated by the clinical target. (See page 404, paragraph 3). He also stated that there is a significant variation that exists in the genetically marked cells recovered from recipients in *ex vivo* studies, emphasizing the unpredictability in the art. (See page 405, col. 3, paragraph 3). Crystal explicitly states that results even in ex vivo methods are inconsistent. (See page 409, col. 1 lines 41-43).

Applicant's argue that "any virus is capable of introducing exogenously the desired DNA to APC cells can be used". However, as stated in the FOAM, being a new field, the state of the prior art does not teach one skilled in the art how to transfer a gene and induce expression at a level sufficient to achieve a therapeutic response with each and every viral vector. Applicant's directed examiner to page 7 of specification, which, contrary to applicant's argument, specifically state applicant's prophetic statements of the ability of any viral vector to transfer the gene of interest. This confirms that applicants are not enabled for each and every viral vector.

The specification describes the construction of a recombinant plasmid vector containing transgenes inserted, but does not teach how these are to be used for therapy. The specification however contains prophetic statements that another vector namely the Vaccinia virus could be used for therapy. No working examples have been provided.

Though the specification, teaches an expression vector such as $pcDNA_3$ transfected in A20B lymphoma cells that are isolated or cultured, which kills activated T cells by means of the Fas ligand, it does not reasonably provide enablement for APC cells transfected with the vaccinia viral vector in vivo. Nor does it teach how to use cultured cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. The specification does not reasonably provide enablement for APC cells transfected with the vaccinia viral vector for invitro or invivo applications.

The specification does not teach or demonstrate making and using the vaccinia virus useful for therapy.

Applicant's are additionally not enabled for the expression of gene fragments that would induce a therapeutic response. Applicant's direct examiner to page 6 of the specification, which state prophetically that "the extracellular portion of the alpha subunit is believed to comprise epitopes to which most AchR-specific T cells respond". However, this is not considered enabling considering the nature and state of the art, as it is not clear if a part of the gene has the same function as the entire gene, unless it is actually shown to do so.

In view of this, the position of record remains that it would require undue experimentation for one skilled in the art to be able to practice the claimed invention of ex vivo gene therapy. Hence, since one skilled in the art cannot readily anticipate the results predicted within the subject matter to which the claimed invention pertains, then there is a lack of predictability in the art.

***Conclusion***

4. Claims 41-67 are rejected.

5. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Deborah Clark

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